to be less frequent in occurrence than *original combinations*, but they are not.

The somatic character of the individual homozygous for two rex genes, r_2 and r_3, is of interest. Each of these genes, by itself, is able to produce the same short-haired type. Together they produce apparently no greater effect than each would produce by itself.

Summary.—Three races of short-haired (rex) rabbits have originated, each by a recessive mutation in a different gene. The genes responsible for two of these rex mutations (r_1 and r_2) are borne in the same chromosome, since they are linked with about 10 or 12 per cent of crossing-over between them. The gene for the third rex mutation (r_3) lies in a different chromosome, since it recombines freely with both r_1 and r_2.

[1] In Nachtsheim's laboratory the genetic symbols used are:

rex = Franz. Rex = r_1
dek = Deutsch-Kurzhaar = r_2
nok = Normannen-Kurzhaar = r_3.

THE GENE THEORY IN RELATION TO BLENDING INHERITANCE

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Before the rediscovery of Mendel's law, Francis Galton had recognized two sharply distinct classes of inherited characters, those which are alternative and those which blend. He found examples of these in human eye color and human stature, respectively. When the parents differ in eye color, the children are like one or the other parent, the inheritance being characterized as alternative; but when the parents differ in stature, the children are of intermediate stature, a blending effect.

With the rediscovery of Mendel's law, it was recognized that an adequate explanation had been found for the inheritance of alternative characters, which were then commonly called unit-characters. But this terminology later fell into disrepute because it was found that literal-minded individuals conceived of the character itself as being inherited in the gametes rather than a single something which was necessary for the production of the character. So the term *gene* was introduced to designate the indispensable something in the germ cell necessary for the development of the character in the individual.

By a brilliant series of discoveries, Morgan and his pupils proved that the genes are located in the chromosomes of the germ cells where they

have a definite arrangement in linear order. The problem of heredity was thus *solved*, as Morgan stated in one of his publications, but only as regards what Galton termed alternative characters. As regards the inheritance of blending characters, a problem still remained unsolved. To its solution I had devoted considerable attention, even before the establishment of the chromosome theory. I found that body size in rabbits behaves as a blending character, regularly producing intermediates, like human stature, according to Galton. This is the unquestionable result in a great number of quantitatively varying characters in animals and plants; and, in general, it is the more fundamental and essential characters of organisms which blend in their inheritance, whereas the more superficial and inconsequential characters mendelize. Accordingly, an understanding of the nature of blending inheritance is of prime importance.

A hypothesis that blending characters, as well as alternative characters, are determined by chromosomal genes gradually gained acceptance, based primarily on the experimental work of Nilsson-Ehle, East and Emerson, and many others. It rests on the following assumptions: (1) that genes located in many different chromosomes affect such a quantitatively varying character as body size; (2) that they are inherited independently, but (3) that their action is cumulative or additive. Thus, genes *ABCD* produce a large animal. *BCD* produce a smaller one, *CD* a still smaller, and so on. This so-called multiple factor explanation of blending inheritance is ingenious and plausible and, at present, generally accepted among students of genetics, but it lacks demonstrative proof. For many years I have sought critical evidence for or against it in crosses between large-bodied and small-bodied races of rabbits, but thus far in vain. I have only negative evidence of the existence in the chromosomes of genes influencing body size. Nevertheless, I have little doubt that they exist. We know that chromosomal genes influence the size, both absolute and relative, of particular parts of the body in animals, and of parts such as leaves, stems and fruits in plants. Thus there is in one race of mice a mutated gene which produces an abnormally short ear. It is borne in the same chromosome as a gene which produces a blue rather than a black coat. There is in mice another mutated gene which produces a generally dwarfed body through reduced activity of the anterior pituitary gland. Both of these genes are inherited in regular alternative mendelian fashion. These cases prove only that body size may be *influenced* by chromosomal genes; they do not prove that the size of an organism is regulated *exclusively* by the action of genes, which is the assumption underlying the gene theory. There has to be an organism before influences can change it in any way. The organism is, I believe, more than a bundle of influences, just as a man is something more than a bundle of endocrine

glands, even though these may profoundly influence his personality and behavior.

The gene theory ignores certain of the findings of embryology which run counter to it. Thus Conklin, Spemann and others have shown that an organization is present in the cytoplasm of the egg at the beginning of development which determines, in a general way, what organs and tissues shall arise from each part of it. The determination is not at first complete and final but becomes progressively more so as development proceeds. In the amphibian egg, at the outset of development, a center of organization, the so-called organizer, determines what organ system shall arise from each of the adjacent parts of the egg. If the organizer is removed from its usual position to another part of the same egg or of a different egg, even to an egg of another species, it still has the power to organize adjacent structures into an amphibian embryo. This is not gene action, for all cells of the embryo have by hypothesis the same gene constitution, irrespective of whether they lie within or without the organizer territory. It is action by the cytoplasm directed by a cytoplasmically differentiated organizer.

But the gene theory holds that the cytoplasmic organization was itself impressed on the cytoplasm by the genes within its nucleus. This is an unproved assumption, for only amphibian cytoplasm containing amphibian genes can produce an amphibian embryo. Both are indispensable, and neither can function without the other. There is no reason to think that historically either has ever existed except in association with the other.[1] Genes may indeed change by mutation, singly or in groups, and thus alter the character of the organism. The cytoplasm also undergoes slow changes, since it has a specifically different character in species or genera which presumably had a common ancestry. But there is no more reason for supposing that cytoplasmic changes are initiated in the gene complex than for the contrary assumption that gene changes originate in the cytoplasm. The studies of Wettstein on plasmatic inheritance in mosses indicate that foreign chromosomes have no modifying action on the cytoplasm even when introduced into it generation after generation.

There is an undoubted mechanism for the inheritance of mendelizing characters in the chromosomes. From the behavior of the chromosomes in fertilization and in maturation of the gametes, alternative inheritance is the only possibility when maternal and paternal gametes differ in their gene content. But blending inheritance is not primarily gene determined unless, as commonly assumed, it is indirect and *masked* gene inheritance, an assumption as yet unproved.

The cytoplasm offers a mechanism suitable for the inheritance of blending characters. The general organization characteristic of the species is already present in the cytoplasm of the egg before fertilization. The

sperm introduces in its chromosomes potential modifiers of this organization which act as accelerators or inhibitors of particular processes in the developing organism, but do not affect the general features of that organization. A similar set of modifiers was already present in the egg pronucleus. The fertilized egg will develop under the joint influence of the two sets of modifiers. If those two sets are exactly alike, gene for gene, then the organism will be completely homozygous and as similar to the mother as asexually produced offspring would be, for it would have cytoplasm derived presumably without change from the mother (or from both parents jointly), and its gene equipment would be identical with that of the mother, provided the mother was also homozygous.

If, however, the two sets of genes are different in any respect, then the modifiers of the organism will be different from those found in the mother. Even though the cytoplasm is identical in character in mother and offspring, the difference in genes acting upon it in the two cases will produce a different result in each.

If the sperm introduces cytoplasm as well as chromosomes into the egg at fertilization (a matter at present uncertain), then there must be a blending of plasms which would account for the blending character in inheritance of general features of organization, such as body size.

Blending characters are the more important and essential ones, those which characterize species, genera and families. Alternative characters (gene determined) as a rule characterize individuals and are more special in nature. There are indeed cases in which Linnean species have been shown to differ by one or more mendelizing characters, but these are rather accidental differences than otherwise. Species crosses usually result in blending inheritance of the general characters of the organism, even when a mendelizing character difference is also involved. The former are the usual and essential differences, the latter are rare and relatively non-essential.

In favor of the hypothesis that blending characters are gene determined is often cited the fact that, as a rule, F_2 is more variable (fluctuates more widely) than F_1. This is assumed to be a consequence of the recombination of multiple factor genes, which undoubtedly act as modifiers of the character in question. But these modifiers may be less important than the organization modified, which finds its expression in the cytoplasm itself. There is reason to believe that the general organization is primarily plasmatic and is derived either from the mother alone or from both parents, if the sperm contains cytoplasm.

On this view racial differences in body size might be due in part to plasmatic differences and in part to gene differences but the increased variability of F_2 as compared with F_1 would be due to gene differences

alone, since blending of plasmas would presumably be as complete in F_2 as in F_1.

In so far as size inheritance is plasmatic, there should be a difference between reciprocal crosses of large-bodied and small-bodied races, since it is reasonable to suppose that the egg plasm is more influential, as it is more abundant, than any cytoplasmic contribution of the sperm. Consequently, we should expect the mother to be more influential than the father in determining the body size of the offspring. In reciprocal crosses between horse and ass this is reported to be true, but the correctness of the report has been challenged, and it must be regarded, for the present, as lacking critical verification. I have reported no difference as being found between reciprocal crosses of large race and small race rabbits, but the number of observations on offspring of small race mothers was small, and no great attention, at the time, was given to the matter which merits renewed investigation.

Summary.—The chromosomes are the undoubted mechanism for the transmission of characters which follow Mendel's law in inheritance. But the more general features of organization are not so inherited. They follow a law described by Galton as blending inheritance. The cytoplasm of the egg-cell affords a suitable mechanism for the transmission of blending characters, although it must be recognized that genes borne in chromosomes may modify such characters. Evidence is needed as to whether the sperm as well as the egg functions in plasmatic inheritance.

[1] In plants such as mosses, where the male gamete resembles an animal spermatozoon in structure, the inheritance has been shown by Wettstein in certain wide species crosses to be such that only maternal chromosomes in maternal cytoplasm are viable, paternal chromosomes in maternal cytoplasm being not viable in the haploid state, though they persist and exert a somatic influence in the diploid generation.

THE EFFECT OF X-RAY DOSAGE ON STERILITY AND NUMBER OF LETHALS IN DROSOPHILA MELANOGASTER

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Abundant evidence is available to show that the effect of x-rays on sterility and on the production of lethals is proportional to the dosage applied. Scattered data dealing with this subject have been summarized in papers appearing recently (Timofeeff-Ressovsky, 1931; Oliver, 1934). From the material published it is evident that standards used in measuring